REMARKS

Claims 1-28 are pending in this application and claims 6-9 and 12-28 are withdrawn from consideration. By this Amendment, claims 1-28 and the specification are amended. The amendments to the specification correct typographical errors, add section titles and add information regarding the deposits of the bacterium and the hybridoma. The amendments to the claims correct typographical errors and place the claims in proper U.S. format. No new matter has been added by this Amendment.

I. Formal Matters

A. Restriction/Election

The Examiner withdrew claims 6-9 and 12-28 from consideration, despite Applicants' election of Group I containing claims 1-5, 10, 11, 16, 17, 25 and 26, according to the September 11, 2003, Restriction Requirement.

Regarding claims 16, 17 and 26, after Applicants elected Group I containing these claims, the Examiner determined that claims 16 and 17 should be placed in non-elected Group V, originally placed in both Groups I and III, and that claim 26 should be placed in non-elected Group VI. The Examiner's decision to remove claims from the elected group and put them into non-elected groups is not based on a typographical error or simple oversight, but is based on a reevaluation of the initial Restriction Requirement. Instead of choosing *sua sponte* the claims under examination (since Applicants already decided to prosecute claims 16, 17 and 26, as members of elected Group I), the Examiner should have provided and therefore should now provide Applicants with the opportunity to elect claims for examination based on the reevaluated Restriction Requirement.

Regarding claim 25, according to the Examiner, originally elected claim 25 depends from claim 14, and thus claim 25 should be placed in non-elected Group VI. However, Applicants note that claim 25 depends from claim 4, *not* claim 14. Since claim 4 is under

examination and since claim 25 was originally a member of elected Group I, Applicants respectfully request that the Examiner place claim 25 back into Group I for examination.

The Examiner stated that the claims of Group I, III, IV, V and VI, presumably, claims 1-17, 25 and 26, are based on the "concept 'bacterium' [which] may link" the Groups, but that this "concept does not constitute a special technical feature" in view of Schoedon et al. (*The Journal of Infectious Diseases 176*: 672-77 (1997)) ("Schoedon") (Office Action, page 3). However, as noted below, Schoedon fails to disclose a reproducible, enabled method for isolating and culturing *Tropheryma whippelii* as evidenced by the fact that the bacteria remained elusive until Applicants' invention. Thus, claims 1-17, 25 and 26 are linked (as acknowledged by the Examiner) by the same special technical feature, i.e., the *novel* bacterium, to form a single inventive concept. Under the lack of unity provisions in an application filed under 35 U.S.C. §371, when the claims are directed to a single inventive concept, there is no lack of unity and a Restriction Requirement is improper.

Applicants note that, on page 3, third full paragraph, of the Office Action, the Examiner stated that the special technical feature of Group III is an antibody. However, this contradicts the Examiner's statement in the second full paragraph on page 3, wherein the linking concept, i.e., special technical feature, of Group III is recited as the bacterium as described above. Applicants agree with the Examiner's initial assessment of the special technical feature of Group III - it is the bacterium, which links all claims 1-28.

Similarly, on page 3, fourth full paragraph, of the Office Action, the Examiner stated that the special technical feature of Groups IV, V and VI "is considered to be different methods using antibodies" (Office Action, page 3). However, again, this contradicts the Examiner's statement in the second full paragraph on page 3, wherein the linking concept, i.e., special technical feature, of Groups IV, V and VI is recited as the bacterium as described

above. Applicants agree with the Examiner's initial assessment of the special technical feature of Groups IV, V and VI - it is the bacterium, which links all claims 1-28.

Regarding Groups II and VII, it is the Examiner's position that the special technical feature of the claims in Groups II and VII is nucleic acid. However, claims 18-22 and 24, the members of Group II, and claims 23, 27 and 28, the members of Group VII, are respectfully directed to a fragment of an *rpoB* gene of *Tropheryma whippelii* and to methods of determining the presence or absence of *Tropheryma whippelii* using at least a fragment of the sequence set forth in SEQ ID NO:3. Thus, contrary to the Examiner's assertion, the special technical feature, i.e., linking concept, *is the bacterium*, which is also the special technical feature of Groups I, III, IV, V and VI. As noted above, when claims in an application filed under 35 U.S.C. §371 are directed to a single inventive concept, there is no lack of unity and a Restriction Requirement is improper.

In addition to the arguments set forth above, Applicants assert that the Restriction Requirement is improper in view of the Examiner's reliance on the dependency of the claims in defending the basis for the Restriction Requirement. Determining the presence or absence of unity of invention is assessed in relation to the independent claims and dependent claims in a different "category of claim," i.e., product, process, apparatus, etc. (MPEP §1850(a)). The dependent claims in the same "category of claim" as the respective independent claims, even if they contain a further invention, do not carry any weight in terms of unity of invention (MPEP §1850(a)).

In the current application, the independent claims are claims 1, 6 and 14. Dependent claims in the same "category of claim" as elected independent claim 1, i.e., product, are claims 2, 3, 18-22, 24 and 27. Thus, it is unclear why the Examiner divided the claims into the seven groups established in the September 11, 2003, Restriction Requirement and reevaluated in the January 28, 2004, Office Action. Clearly, the Restriction Requirements in

both Office Actions fail to follow the unity of invention provisions and fail to support the Examiner's claim that unity of invention is lacking in this application.

In view of the arguments set forth above, withdrawal of the Restriction Requirement is respectfully requested.

B. Specification Informalities

The Examiner stated that the specification is not in the arrangement required by 37 C.F.R. §1.77(e) and does not contain section titles.

In response, Applicants added section titles to the specification as requested. Applicants note that, contrary to the Examiner's comment regarding the lack of a brief description of the drawings, there is a brief description of the drawings on page 15 of the specification.

The Examiner stated that the claims should begin with the appropriate title of "I Claim," "We Claim" or "What Is Claimed" and should be the subject of a complete sentence. In response, Applicants note that the claims now read as complete sentences and are entitled "We Claim."

The Examiner referred to claim 5 and its recitation of molecular weights determined in the figures as inaccurate terminology. In response, Applicants amended claim 5 such that the figures are not recited therein.

Applicants have complied with the requested changes to the specification and claims.

C. Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-5, 10 and 11 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. Applicants respectfully traverse the rejection.

The Examiner stated that the specification lacks complete information for the deposit of the bacterium, CNCM I-2202, and for the hybridoma, CNCM I-2411. According to the Examiner, it is not clear if the bacterium and hybridoma are known and publicly available or whether they can be reproduced from nature without undue experimentation.

The bacterium, CNCM I-2202, was deposited in accordance with the Budapest Treaty on May 19, 1999, at the Collection Nationale de Cultures de Microorganismes (CNCM). Similarly, the hybridoma, CNCM I-2411, was deposited in accordance with the Budapest Treaty on March 22, 2000, at the CNCM. A copy of the receipts for the deposits of the bacterium and the hybridoma is attached hereto. All restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and the deposits will be replaced if viable samples cannot be dispensed by the depository. The specification now recites the dates of deposit and the complete name and street address of the depository.

Since Applicants made the deposits under the provisions of the Budapest Treaty and amended the specification to recite the address of the depository and deposit dates, Applicants have satisfied the requirements of 35 U.S.C. §112, first paragraph. Applicants respectfully request withdrawal of the rejection.

D. Rejection under 35 U.S.C. §112, Second Paragraph

Claims 5 and 11 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Applicants respectfully traverse the rejection.

The Examiner stated that claim 5 is vague and indefinite due to the recitation of "molecular weights of about 35, 50, 60, 100 and 200 kD determined in Figures 2 and 3." The Examiner stated that molecular weights in claims to characterize a protein should include the

method by which the molecular weight was determined as well as whether the determination was made under denaturing conditions or reducing conditions.

Applicants agree that they are required to distinctly claim the subject matter regarded as the invention. However, Applicants are not required to include details from the specification since claims are read in light of the specification, nor are Applicants required to include details of well-known concepts in the claims (or even in the specification). One of ordinary skill in the art understands the concept of molecular weights and knows how they are determined. Regardless, without acquiescing in the propriety of the rejection, but solely to expedite prosecution, Applicants amended claim 5 by removing the reference to Figures 2 and 3. Thus, amended claim 5 states that the recited molecular weights are determined by polyacrylamide gel electrophoresis using the well-known technique of Western blotting, which is described in the specification in Example 6.

Regarding claim 11, the Examiner stated that the claim does not recite process steps that relate to the purpose of the method as set forth in the preamble. In response, without acquiescing in the propriety of the rejection, but solely to expedite prosecution, Applicants amended claim 11 such that the claim recites process steps that correlate to the intended purpose as set forth in the preamble.

Based on the arguments set forth above and the amendments to claims 5 and 11, withdrawal of the rejection is respectfully requested.

E. <u>Rejection Under 35 U.S.C. §102(b)</u>

Claims 1, 2 and 4 are rejected under 35 U.S.C. §102(b) as being anticipated by Schoedon et al. (*The Journal of Infectious Diseases 176*: 672-77 (1997)) ("Schoedon"). Applicants respectfully traverse the rejection.

The Examiner characterized Schoedon as disclosing the isolation of *Tropheryma whippelii*, which is responsible for Whipple's disease, from a biopsy sample from an infected

patient. According to the Examiner, the bacteria were cultured in medium containing deactivated monocular phagocytes, and thus Schoedon teaches the isolation and cultivation of *Tropheryma whippelii* and anticipates claim 1. Regarding claim 2, the Examiner stated that claim 2 is product-by-process claim, and thus Schoedon anticipates the claim due to the disclosure of the isolation and cultivation of *Tropheryma whippelii* as applied to claim 1. The Examiner asserted that the process set forth in claim 2 is not relevant to the product of claim 2 since the patentability of a product does not depend on the method of production recited in the claim. Regarding claim 4, the Examiner referred to Figure 5 in Schoedon and stated that, "Figure 5 would read on antigen of bacterium as periodic acid-Schiff inclusion in bacterium has been identified" (Office Action, page 10).

Applicants acknowledge that Schoedon appears to describe isolating and culturing *Tropheryma whippelii*. However, after Schoedon was published, it was publicly acknowledged that *Tropheryma whippelii* cannot be isolated and cultured under the conditions established by Schoedon and that Schoedon's work was unsuccessful. Since Schoedon's work cannot be reproduced, the reference is not enabled, and thus cannot anticipate the subject matter claimed.

According to the MPEP §2121, prior art relied on to anticipate a claimed invention must be enabling. A reference contains an enabling disclosure if the public was in possession of the claimed invention before the date of the claimed invention. In this case, Schoedon fails to put the public in possession of isolated and cultured *Tropheryma whippelii* as evidenced by Raoult et al., *The New England Journal of Medicine 342:*620-25 (2000) (Didier Raoult, the first named inventor on the subject patent application, is the corresponding author), and Hinrikson et al., *International Journal of Systematic Bacteriology 49:*1701-06 (October 1999) (both references cited in the IDS filed May 15, 2002).

Regarding Hinrikson et al., the authors refer to *Tropheryma whippelii* as "the uncultivated causative agent of Whipple's disease" (abstract). Hinrikson et al. further notes that, in 1999, DNA-DNA hybridization studies, although needed, were not feasible because *Tropheryma whippelii* had not been cultured yet on artificial media (page 1706, col. 1). It is telling that Hinrikson et al. lists the corresponding author as Martin Altwegg - an author on the Schoedon et al. reference published two years prior to the publication of Hinrikson et al. Fabrizio Dutly is also an author on both publications.

Similarly, Raoult et al. was published March 2, 2000, over three years after the publication of Schoedon, yet Raoult et al. describes *Tropheryma whippelii* as "an elusive goal for many generations of microbiologists" (page 620, col. 2). Raoult et al. cites Schoedon, stating that, in 1997, the publication year of Schoedon, *Tropheryma whippelii* was isolated and grown, but that the isolate could not be subcultured, and thus no isolate was previously available. More specifically, Raoult et al., in reference to Schoedon's work, stated that, "[u]nlike previous investigators who completed only two passages of the bacterium cultures of human macrophages, we [Raoult et al.] used a human fibroblast cell line with no specific culture conditions [and] . . . . completed seven passages of our isolate[, thus we] . . . believe that the culture is now definitely established" (page 624, col. 1). Clearly, Applicants have succeeded where Schoedon failed by successfully isolating and culturing *Tropheryma whippelii* as claimed. Submitted herewith as additional evidence in support of Applicants' arguments are copies of several requests for samples of the successfully isolated and cultured *Tropheryma whippelii* (Deposit No. I-2202), deposited by Applicants in the CNCM.

Raoult et al. and Hinrikson et al. invalidate Schoedon's work a few years after Schoedon was published. However, even at the time that Schoedon was published, those of ordinary skill in the art doubted Schoedon's claims. For example, in the *same* journal as Schoedon, David A. Relman, *The Journal of Infectious Diseases 176:*752-54 (1997) (attached

hereto), in a Commentary on Schoedon's work, states that, "the findings reported herein [Schoedon] need to be reproduced by others" (page 753, col. 2, last paragraph). Dr. Relman further states that Schoedon's "report" requires careful evaluation since "[i]n the absence of direct bacterial quantification and any obvious extracellular growth in vitro, how strong is the evidence for microbial replication? . . . PAS [periodic acid-Schiff] reactivity is difficult to quantitate and is only an indirect marker of bacterial number . . . [and] the details of [PCR] assay specificity are not provided" (page 752, col. 2, first full paragraph, to page 753, col. 1, first full paragraph). Schoedon relied upon results generated from PAS inclusions and PCR-based assays to substantiate the claims of microbial growth.

Schoedon's failure can be explained, at least in part, by the fact that the cells Schoedon used were human blood monocytes, which do not multiply and do not survive beyond thirty days, and thus cannot support a bacterial culture (specification, page 2, lines 19-24). Problems with the cell culture conditions chosen by Schoedon were alluded to in the Commentary, wherein Dr. Relman states that, "[t]he cell cocultivation conditions . . . may have biased the outcome toward intracellular survival and growth and may not have provided the bacterium with the extracellular conditions that it encounters and prefers in a susceptible host" (page 753, col. 2, second full paragraph).

Regarding claim 4, since *Tropheryma whippelii* was not available prior to Applicants' work, it follows that the antigen thereto was also not previously available.

In view of the arguments set forth above, withdrawal of the rejection is respectfully requested.

II. Information Disclosure Statement

An Information Disclosure Statement with Form PTO-1449 was filed in the above-captioned patent application on December 5, 2001. Applicants appreciate the Examiner's consideration of the non-patent publications cited on the Form PTO-1449. Applicants request

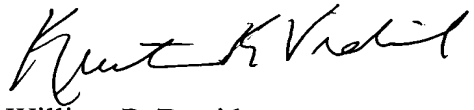
that the Examiner also consider the patent cited on the Form PTO-1449 and initial the Form to acknowledge the fact that the Examiner has considered all of the disclosed information. The Examiner is requested to initial and return to the undersigned a copy of the completed Form PTO-1449. For the convenience of the Examiner, a copy of the original Form and the Examiner's initialed form is attached.

III. Conclusion

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of all claims are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,



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WPB:KKV/amw

Attachments:
- Abstract
- Copy of Form PTO-1449, dated December 5, 2001, and Examiner's initialed Form
- Copy of receipts from the CNCM Depository for Deposit Nos. I-2202 and I-2411
- Copy of Relman, D.A., *The Journal of Infectious Diseases 176:*752-54 (1997)
- Copy of requests for *Tropheryma whippelii* Deposit No. CNCM I-2202

Date: April 28, 2004

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